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RECOMBINANT NEGATIVE STRAND RNA VIRUS EXPRESSION SYSTEMS AND VACCINES

This is a continuation-in-part of application Serial No. 08/190,698, filed February 1, 1994, which is a continuation of application Serial No. 07/925,061, filed August 4, 1992 (abandoned), which is a divisional of application Serial No. 07/527,237, filed May 22, 1990 (issued as U.S. Patent No. 5,166,057), which is a continuation-in-part of application Serial No. 07/440,053, filed November 24, 1989 (abandoned), which is a continuation-in-part of application Serial No. 07/399,728, filed August 28, 1989 (now abandoned).

1. INTRODUCTION

The present invention relates to recombinant negative strand virus RNA templates which may be used to express heterologous gene products in appropriate host cell systems and/or to construct recombinant viruses that express, package, and/or present the heterologous gene product. The expression products and chimeric viruses may advantageously be used in vaccine formulations.

The invention is demonstrated by way of examples in which recombinant influenza virus RNA templates containing a heterologous gene coding sequences in the negative-polarity were constructed. These recombinant templates, when combined with purified viral RNA-directed RNA polymerase, were infectious, replicated in appropriate host cells, and expressed the heterologous gene product at high levels. In addition, the heterologous gene was expressed and packaged by the resulting recombinant influenza viruses.

2. BACKGROUND OF THE INVENTION

A number of DNA viruses have been genetically engineered to direct the expression of heterologous proteins in host cell systems (e.g., vaccinia virus, baculovirus, etc.). Recently, similar advances have been made with positive-strand RNA